

Appln. No.: 09/435,249  
Reply to Office Action dated May 7, 2003

Atty. Docket No. 8321-111

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listing, of claims in the application:

#### **Listing of Claims**

Claim 1: (Previously amended): A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of antisense oligonucleotide comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 to the substantia nigra pars reticulata via a cannula for the downregulation of glutamic acid decarboxylase.

Claim 2 (Original): The method of claim 1 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>65</sub>.

Claim 3 (Original): The method of claim 1 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>67</sub>.

Claim 4 (Currently amended): The method of claim 1 wherein the isoform of said glutamic acid decarboxylase is a combination of GAD<sub>65</sub> and GAD<sub>67</sub>.

#### **Claims 5-8 (Previously cancelled)**

Claim 9 (Previously amended): A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of antisense oligonucleotide comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 to the internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase.

Claim 10 (Original): The method of claim 9 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>65</sub>.

Claim 11 (Original): The method of claim 9 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>67</sub>.

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Claim 12 (Original): The method of claim 9 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>65</sub> and GAD<sub>67</sub>.

Claims 13-29 (Previously cancelled)

Claim 30 (Cancelled)

Claims 31-33 (Previously cancelled)

Claims 34-37 (Cancelled)

Claim 38 (New): A method of downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide directed to an initiation codon of glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula, wherein said antisense oligonucleotide comprises SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, or SEQ ID NO: 5.

Claim 39 (New): The method of claim 1, wherein the oligonucleotide comprises phosphorothioate linkages.

Claim 40 (New): The method of claim 9, wherein the oligonucleotide comprises phosphorothioate linkages.

Claim 41: (New): The method of claim 38, wherein the oligonucleotide comprises phosphorothioate linkages.